



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re patent application of
Schmidt-Ullrich and Valerie

Serial No. 09/741,790 Examiner Chen

Filed 11/17/2000 Art Unit 1632

For "GENETIC INHIBITION OF EPIDERMAL GROWTH"

For "GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR
FUNCTION AND CARCINOMA CELL RADIOSENSITIZATION"

**Assistant Commissioner of Patents
Washington, D.C. 20231**

DECLARATION UNDER 37 C.F.R. § 1.132

Geoffrey D. Bowers declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed


Geoffrey D. Bowers

Date 3-25-03



In re patent application of

Schmidt-Ullrich and Valerie

Serial No. 09/741,790

Examiner Chen

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For "**GENETIC INHIBITION OF EPIDERMAL GROWTH FACTOR RECEPTOR
FUNCTION AND CARCINOMA CELL RADIOSENSITIZATION**"

Assistant Commissioner of Patents
Washington, D.C. 20231

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TECH CENTER 1600/2900

DECLARATION UNDER 37 C.F.R. § 1.132

Joseph N. Contessa declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed


Joseph N. Contessa

Date

3/20/03



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Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Paul Dent declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed

Paul Dent

Date 3/18/03



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Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Ross B. Mikkelsen declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed 
Ross B. Mikkelsen

Date 3/10/03



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Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Dean B. Reardon declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed

Dean B. Reardon

Date 3/24/03



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Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132

Daniel Todd declares as follows:

1. I am a co-author of the publication Contessa et al., *Clinical Cancer Research* 5:405-11, 1999.
2. I have reviewed United States patent application 09/741,790, including the claims.
3. I am not an inventor of the subject matter which is claimed in 09/741,790.
4. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the above-referenced application and any patent issuing thereon.

Signed

Daniel Todd

Date

3/25/03

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DECLARATION UNDER 37 C.F.R. 1.131

Dr. Rupert Schmidt-Ullrich and Dr. C. Kristoffer Valerie declare as follows:

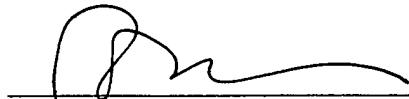
1. I, Dr. Rupert Schmidt-Ullrich, am professor and chair of the Department of Radiation Oncology at Virginia Commonwealth University; and I, Dr. C. Kristoffer Valerie, am a professor in the Department of Radiation Oncology at Virginia Commonwealth University.
2. Virginia Commonwealth University is the assignee of the above-referenced United States patent application.
3. We are the sole inventors of the subject matter claimed in the above-referenced United States patent application.
4. We are joint authors of the reference article Contessa et al., *Clinical Cancer Research* 5:405-11, 1999. The other authors of the article are not inventors of the subject matter claimed in the above-referenced United States patent application.

5. As evidence of possession of the invention prior to the date of publication of the reference article, we herewith submit a copy of the original manuscript of the article which was submitted to *Clinical Cancer Research*, together with a copy of the letter of submission. Both documents were created prior to the publication date of the Contessa et al. article. On the bottom left of the front page of the manuscript, there is a hand-written indication that the manuscript was received by the journal. The date of receipt is prior to the publication of the Contessa et al. article. The manuscript contains all the information of the final publication of Contessa et al, as well as demonstrates our possession of the invention now claimed., including the concept of utilizing the dominant negative construct to transduce cancer cells in order to radiosensitize them. This is stated, for example, in the last two sentences of the abstract, and the last two sentences of the discussion (page 14 beginning on line 20, and page 15, lines 1-3). Thus, we were in possession of the subject matter of claim 19 and dependent claims 20-23, 25, 29 and 32 at least by the date of submission of the manuscript. In short, the manuscript demonstrates that we had conceived of and tested the invention prior to the publication date of the Contessa et al. article.

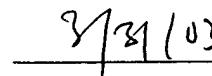
6. We were diligent in reducing the invention to practice from a time prior to the publication of the Contessa et al. publication. Attached is an excerpt of an invention disclosure submitted to the Office of Technology Transfer of Virginia Commonwealth University on July 28, 1999, and a copy of United States provisional patent application 60/165,940 filed November 17, 1999, in which the contents of the university disclosure and the Contessa et al. publication were included. The provisional application was filed less than one year after publication of the Contessa et al. article. In the disclosure and in the provisional application, the concept of utilizing an EGFR dominant negative mutant to radiosensitize cancer cells was discussed.

7. We declare further that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true and further that these statements are made with the knowledge that willful false statements and the like so made are

punishable by fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.



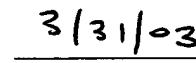
Rupert Schmidt-Ullrich



Date

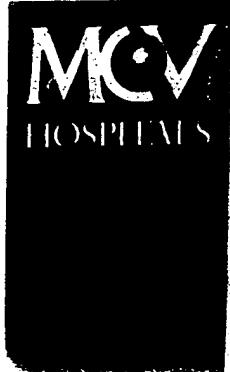


C. Kristoffer Valerie



Date

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Reston, VA 20190
703-787-9400



Virginia Commonwealth University

**DEPARTMENT OF
RADIATION ONCOLOGY**

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904 828-7238
FAX: 904 828-6042
TDD: 1-800 828-1120

RUPERT SCHMIDT-ULLRICH, M.D.,
PROFESSOR AND CHAIRMAN
FACR

June 24, 1998

**Dr. John Mendelsohn, M.D., Editor-in-Chief
Department of Educational Publishing Services-227
The University of Texas M.D. Anderson Cancer Center
1515 Holcombe Boulevard
Houston, TX 77030**

Dear Dr. Mendelsohn:

Enclosed I am sending the manuscript entitled "The Inducible Expression of Dominant Negative EGFR-CD533 Results in Radiosensitization of Human Mammary Carcinoma Cells" by Joseph N. Contessa, Dean B. Reardon, Daniel Todd, Paul Dent, Ross B. Mikkelsen, Kristoffer Valerie, Geoffrey D. Bower, and Rupert K. Schmidt-Ullrich for consideration of publication in Clinical Cancer Research.

Because of potential conflict of interest we suggest that this manuscript not be reviewed by Dr. Ralph Weichselbaum. Instead, we consider Dr. Anatoly Dritschilo, Chairman, Department of Radiation Medicine, Georgetown Medical Center, 3800 Reservoir Road, N.W., Washington, DC 20007 and Dr. Amato Giaccia, Department of Radiation Oncology, Stanford University, GK 115, CBRL, Stanford, CA 94305-5468, as potential additional reviewers for the radiobiological aspects of this manuscript.

Thank you for your consideration.

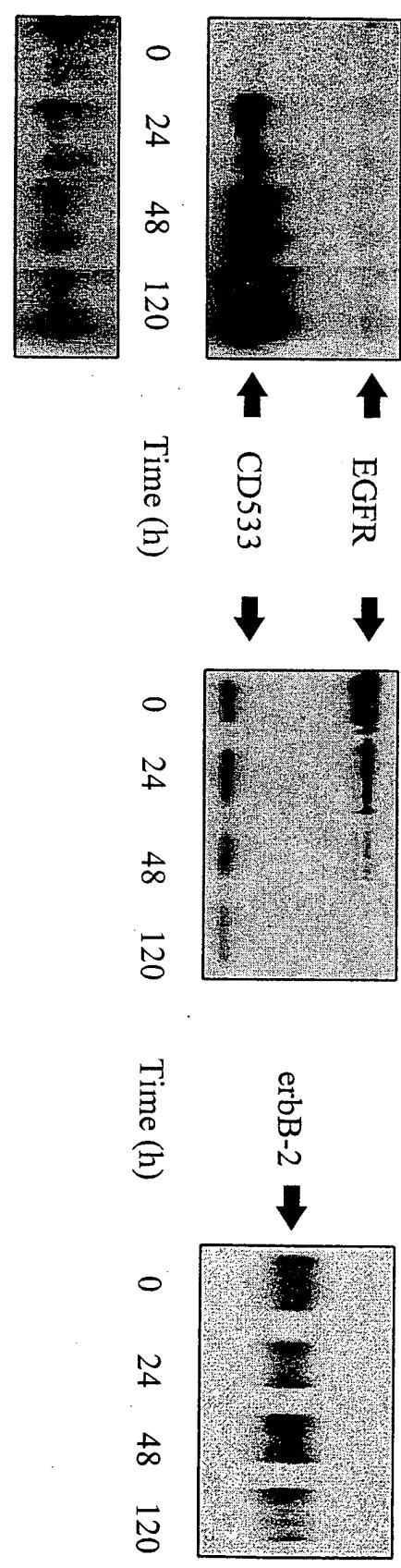
Sincerely,

A handwritten signature in black ink, appearing to read 'Rupert Schmidt-Ullrich'.

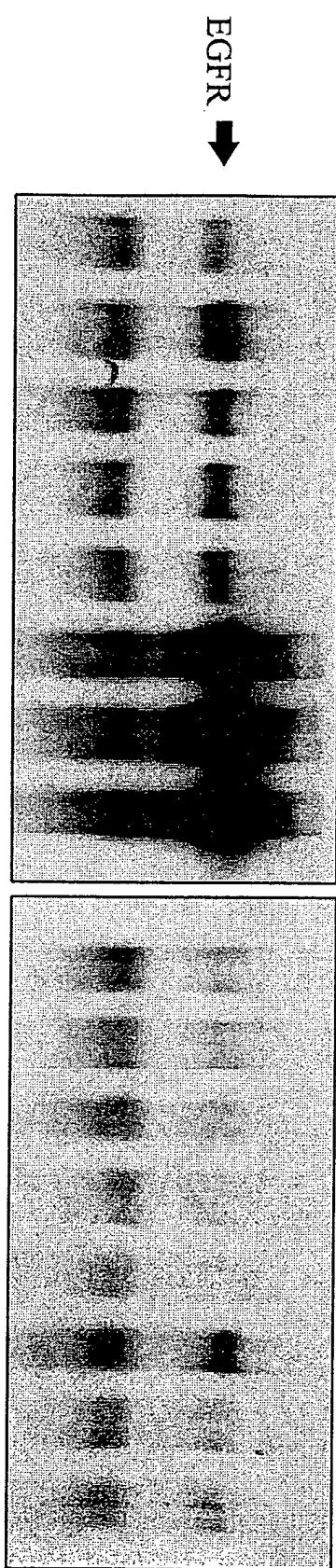
Rupert Schmidt-Ullrich, M.D.

Enclosure

A. EGFR-WT/CD533



D. EGFR-WT Tyr Phosphorylation



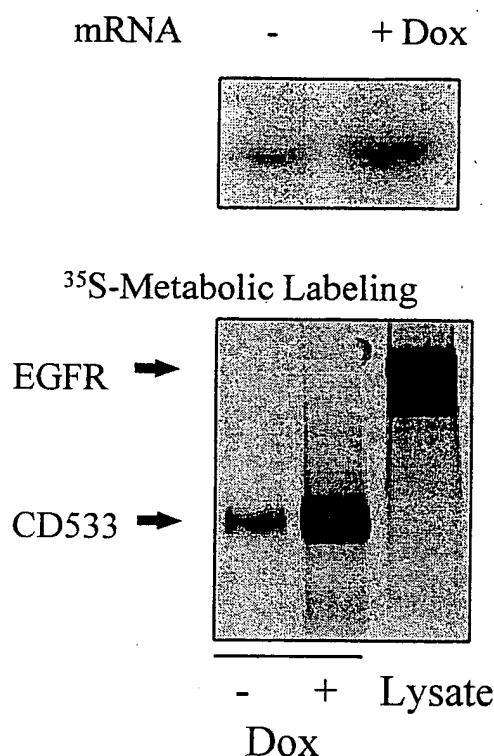
B. EGFR-WT "activated"

C. ErbB-2

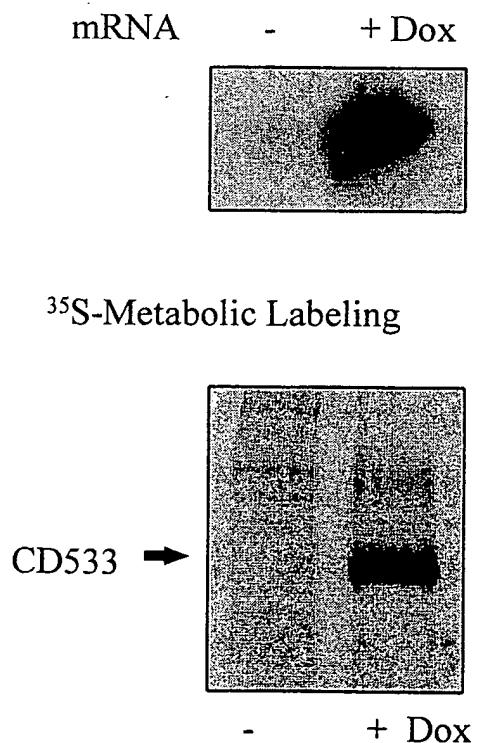
Radiation EGF
- Dox + Dox

383048

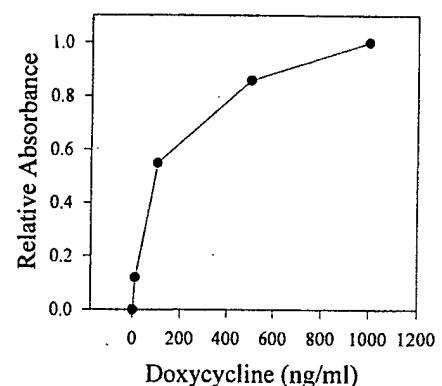
A. MCF-TR5-CD533



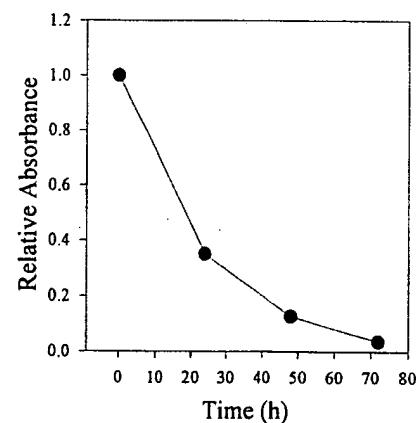
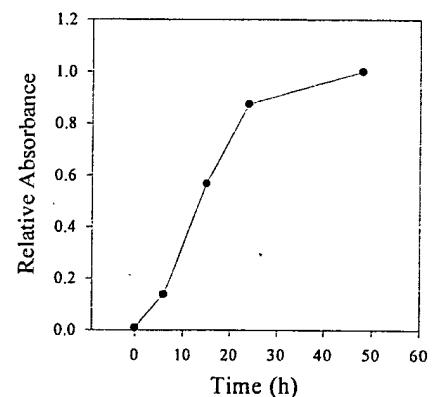
B. MDA-TR15-CD533



C. Dox Dose Response of EGFR-CD533 Expression



D. Induction and Decay of EGFR-CD533 Expression



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